shown: (1) To be capable of concentrating tenfold from source material at least two different antibodies; (2) not to affect the integrity of the globulins; (3) to consistently yield a product which is safe for subcutaneous and intramuscular injection and (4) not to transmit viral hepatitis.

(b) *Microbial contamination.* Low temperatures or aseptic techniques shall be used to minimize contamination by microorganisms. Preservatives to inhibit growth of microorganisms shall not be used during processing.

(c) *Bulk storage.* The globulin fraction may be stored in bulk prior to further processing provided it is stored in clearly identified hermetically closed vessels. Globulin as either a liquid concentrate or a solid and containing alcohol or more than 5 percent moisture shall be stored at a temperature of −10° C. or lower. Globulin as a solid free from alcohol and containing less than 5 percent moisture, shall be stored at a temperature of 0° C. or lower.

(d) *Determination of the lot.* Each lot of Immune Globulin (Human) shall represent a pooling of approximately equal amounts of material from not less than 1,000 donors.

(e) *Sterilization and heating.* The final product shall be sterilized promptly after solution. At no time during processing shall the product be exposed to temperatures above 45°C. and after sterilization the product shall not be exposed to temperatures above 30° to 32° C. for more than 72 hours.

[38 FR 32089, Nov. 20, 1973, as amended at 50 FR 4140, Jan. 29, 1985]

§ 640.103 The final product.

(a) *Final solution.* The final product shall be a 16.5±1.5 percent solution of globulin containing 0.3 molar glycine and a preservative.

(b) *Protein composition.* At least 90 percent of the globulin shall have an electrophoretic mobility not faster than -2.8×10^{-5} centimeters^2 per volt per second, when measured at a 1 percent protein concentration in sodium diethylbarbiturate buffer at pH 8.6 and 0.1 ionic strength.

§ 640.104 Potency.

(a) *Antibody levels and tests.* Each lot of final product shall contain at least the minimum levels of antibodies for diphtheria, measles, and for at least one type of poliomyelitis. In the event the final bulk solution is stored at a temperature above 5° C. the antibody level tests shall be performed after such storage with a sample of the stored material.

(b) *Minimum levels.* The minimum antibody levels are as follows:

(1) No less than 2 units of diphtheria antitoxin per ml.

(2) A measles neutralizing antibody level of no less than 0.50 times the level of the Reference Immune Serum Globulin, except that when recommended for use with Measles Virus Vaccine Live, the measles antibody level shall be as prescribed in § 640.114.

(3) A poliomyelitis neutralizing antibody level of no less than 1.0 for Type 1, 1.0 for Type 2, and 2.5 for Type 3, times the antibody level of the Reference Immune Serum Globulin.

(c) *Reference materials.* The following reference materials shall be obtained from the Center for Biologics Evaluation and Research:

(1) Reference Immune Serum Globulin for correlation of measles antibody titers.

(2) Reference Immune Serum Globulin for correlation of poliomyelitis antibody titers, Types 1, 2, and 3.

[38 FR 32089, Nov. 20, 1973, as amended at 39 FR 9661, Mar. 13, 1974; 49 FR 23834, June 8, 1984; 50 FR 4140, Jan. 29, 1985; 55 FR 11013, Mar. 26, 1990]

Subpart K—Measles Immune Globulin (Human)

§ 640.110 Measles Immune Globulin (Human).

(a) *Proper name and definition.* The proper name of the product shall be Measles Immune Globulin (Human). It shall consist of a sterile solution of 10 to 18 percent globulin derived from human blood, having the same measles antibody level as the Reference Measles Immune Globulin. Measles Immune Globulin shall be made from a sterile 16.5 ±1.5 percent solution of human globulin.

(b) *Source material.* The source of Measles Immune Globulin (Human) shall be blood, plasma or serum from human donors determined at the time of donation to have been free of causative agents of diseases that are not destroyed or removed by the processing method, as determined by the donor's history and from such physical examination and clinical tests as appear necessary for each donor at the time the blood was obtained. The source blood, plasma or serum shall not contain a preservative and shall be stored in a manner that will prevent contamination by microorganisms, pyrogens or other impurities.

(c) *Additives in source material.* Source blood, plasma or serum shall contain no additives other than citrate or acid citrate dextrose anticoagulant solution, unless it is shown that the processing method yields a product free of the additive to such an extent that the safety, purity and potency of the product will not be affected adversely.

[38 FR 32089, Nov. 20, 1973, as amended at 39 FR 9661, Mar. 13, 1974]

§ 640.111 General requirements.

(a) *Heat stability test.* Approximately 2 ml of final container material of each lot shall not show any visible sign of gelation after heating in a 12 × 75 mm. stoppered glass tube at 57° C. for four hours.

(b) *Hydrogen ion concentration.* The pH of final container material shall be 6.8±0.4 when measured in a solution diluted to 1 percent protein with 0.15 molar sodium chloride.

(c) *Turbidity.* The product shall be free of turbidity as determined by visual inspection of final containers.

(d) *Date of manufacture.* The date of manufacture is the date of initiating the last valid measles antibody test as required in § 640.114.

(e)—(f) [Reserved]

(g) *Samples and protocols.* For each lot of globulin, the following materials shall be submitted to the Director, Center for Biologics Evaluation and Research, Food and Drug Administration, 8800 Rockville Pike, Bethesda, MD 20892.

(1) 30 ml of final product.

(2) All protocols relating to the history of the manufacture of each lot and all results of all tests prescribed in these additional standards.

[38 FR 32089, Nov. 20, 1973, as amended at 49 FR 23834, June 8, 1984; 51 FR 15611, Apr. 25, 1986; 55 FR 11013, Mar. 26, 1990]

§ 640.112 Manufacture of Measles Immune Globulin (Human).

(a) *Processing method.* The globulin shall be prepared by a processing method that (1) has been shown to be capable of concentrating tenfold from source material at least two different antibodies, (2) does not affect the integrity of the globulins and is capable of consistently yielding a product which is safe for subcutaneous and intramuscular injections and (3) will not transmit viral hepatitis.

(b) *Reference materials.* The following reference material shall be obtained from the Center for Biologics Evaluation and Research: Reference Measles Immune Globulin for correlation of measles antibody titers with globulin products.

(c) *Microbial contamination.* Low temperatures or aseptic techniques shall be used to minimize contamination by microorganisms. Preservatives to inhibit growth of microorganisms shall not be used during processing.

(d) *Bulk storage.* The globulin fraction may be stored in bulk prior to further processing provided it is stored in well-marked hermetically closed vessels. Purified globulin as either a liquid concentrate or a solid and containing alcohol or more than 5 percent moisture shall be stored at a temperature not to exceed −10° C. Purified globulin as a solid free from alcohol and containing less than 5 percent moisture, shall be stored at temperatures not to exceed 0° C.

(e) *Determination of the lot.* Each lot of Measles Immune Globulin (Human) shall represent a pooling of material from not less than 1,000 donors.

(f) *Sterilization and dilution.* The product shall be prepared initially as a 16.5 percent solution and this preparation shall be sterilized promptly after solution. After sterilization the product shall not be exposed to temperatures above 45° C. for more than a total of 72 hours. Dilution of this sterile globulin